



# KANSAS DRUG UTILIZATION REVIEW NEWSLETTER

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Welcome to the winter 2009 edition of the "Kansas Drug Utilization Review Newsletter," published by Health Information Designs, Inc. (HID). This newsletter is part of a continuing effort to keep the Medicaid provider community informed of important changes in the Kansas Medical Assistance Program (KMAP).

## KMAP Helpful Phone Numbers

### Provider Customer Service: 1-800-933-6593

Press '1' then:

- 0—Customer Service Representative
- 1—Eligibility, NDC Coverage, & Claims Status
- 2—Reset Pin Numbers
- 3—EDI (Electronic Data Interchange)
- 4—Dental Specialist
- 5—Prior Authorization
- 6—Provider Enrollment

### Beneficiary Customer Service:

1-800-766-9012

### Pharmacy Help Desk:

1-866-405-5200

- Pharmacy Claims
- ProDUR
- Drug Coverage Questions

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## Understanding Bioequivalence

People sometimes speculate that brand name medications, being more expensive, are better agents than their generic counterparts. However, this is not the case. The U.S. Food and Drug Administration (FDA) has established a rigorous program to ensure every marketed form of a drug has the same biological effect. When a brand name product comes off patent, drug manufacturers are permitted to develop generic versions. Generic manufacturers, who do not have the significant advertising and research and development costs that brand name manufacturers face, are able to offer their products at a lower price. For a generic drug to be considered bioequivalent to the brand name product, it must be identical in active ingredients, dosage form, safety, strength, quality, and intended use. Generic drugs must also be manufactured under the same FDA standards as brand name products. In fact, many generic drugs are manufactured in the same plants as the brand name product.

Generic drug applications do not require preclinical and clinical data to demonstrate safety and efficacy. This is because the medication has already been proven to be efficacious and safety studies have been performed by the brand name manufacturer. Instead, generic drug manufacturers must demonstrate that their product is bioequivalent to the brand name drug. When a generic drug is approved, it has met standards established by the FDA with respect to identity, strength, quality, purity and potency. When a drug—either brand or generic—is mass produced, small variations in purity, size, strength and other parameters are permitted. The FDA puts limits on how much variability is acceptable. These guidelines are the same for both brand and generic products.

### Proving Bioequivalence

The FDA requires bioequivalence to be calculated using three pharmacokinetic parameters: the maximum concentration (C<sub>max</sub>), the time at which the maximum concentration is reached (T<sub>max</sub>), and the area under the curve (AUC). The rate of absorption is evaluated by measuring the C<sub>max</sub> and the T<sub>max</sub>. The extent of absorption (the amount of drug absorbed) is calculated by measuring the AUC. The brand name product is the reference standard for AUC, C<sub>max</sub>, and T<sub>max</sub>. To be considered bioequivalent, a generic drug must demonstrate that its values for AUC, C<sub>max</sub>, and T<sub>max</sub> are similar to those of the brand name product.

The calculations used to determine the similarity in these pharmacokinetic parameters measuring the rate and extent of absorption involve complex statistics. The calculation requires that the 90% confidence interval for the mean response of the generic drug fall within 80% to 125% of that of the brand name drug, using log-transformed data.

Practically, this confidence interval calculation shows that nine times out of ten, the mean response of an individual (when tested in precisely the same way) would fall within the same numerical limits of the original test. Alternatively, there is only a 10% chance that an individual would have a mean response outside the limits of the original test.

This rule is often misinterpreted or misrepresented as meaning that the mean bioavailability (rather than the 90% confidence interval of the mean response) of the generic drug must be within 80% and 125% of that of the brand product. Because the computation of a confidence interval is influenced by the study design—considering the number of subjects and the intrasubject variability inherent in the bioequivalence testing—the actual differences in AUC or C<sub>max</sub> between test and reference products must be considerably less than -20% to +25%. *Continued on Page 4.*

## Dispense as Written Prior Authorization

According to pharmacy law, if a prescriber specifies dispense as written (DAW) on a prescription the pharmacy may not substitute a generic version for the brand name without prescriber consent. If a pharmacy dispenses a brand name product when a bioequivalent generic is available, they are reimbursed at the multisource product rate (Average Wholesale Price – 27%) rate. This may mean that pharmacies could lose money when dispensing brand name products if a generic product is available.

**“To ensure that beneficiaries have access to care, prescribers are encouraged to write for generic products unless using the brand name product is medically necessary.”**

Pharmacies may charge the beneficiary for the full price of the medication or decline to fill the prescription only in the following three cases:

- The prescriber decides not to fill out and submit an FDA MedWatch form.
- The beneficiary's prior authorization (PA) is denied.
- The beneficiary requests brand name when the prescriber has written for substitution permissible.

When the pharmacy decides to charge the beneficiary the full price of the medication they must first make a 'good faith' effort to attain a DAW prior authorization. The pharmacy must also inform the beneficiary of the possibility they may have to pay the full price of the medication if the DAW prior authorization is denied.

To ensure that beneficiaries have access to care, prescribers are encouraged to write for generic products unless using the brand name product is medically necessary. If the brand name product is medically necessary, a DAW prior authorization is available to ensure beneficiaries have access to the medications they require.

The DAW prior authorization requires that the prescriber submit a completed FDA MedWatch form to both the dispensing pharmacy and the FDA. The dispensing pharmacy should then submit the completed MedWatch form to the Kansas Medical Assistance Program (KMAP) PA unit for evaluation. The form should include the pharmacy name, pharmacy phone and fax numbers, and pharmacy KMAP provider number. The PA unit will contact the pharmacy to inform them of the status of the DAW request.

Not all completed MedWatch forms are approved for coverage. Specific criteria must be met to determine the medical necessity for a brand name product when a bioequivalent generic substitute is available. Currently, there are three criteria that are accepted for approval. These criteria are listed in the table below.

Including the FDA MedWatch form in this PA process helps KMAP increase patient safety, avoid unnecessary expenditures, and assist the FDA in monitoring drug products.

Currently, there are a few drugs for which KMAP requires a separate PA process for pharmacies to obtain reimbursement for the brand name medication. In these instances, the prescriber is not required to complete a FDA MedWatch form; the pharmacy, however, must contact the KMAP PA unit to initiate the process. Brand name drugs included in this process are: Tegretol, Depakene, Mysoline, Klonopin, Ceberclon, Coumadin, and Clozaril.

For more information please refer to the KMAP Provider Manuals located on the KMAP Web site at <https://www.kmap-state-ks.us/public/providermanuals.asp>.

The MedWatch forms and information on submitting forms to the FDA may be found online at <http://www.fda.gov/Safety/MedWatch/HowToReport/DownloadForms/default.htm>.

### One of the following criteria must be met for approval of a Dispense as Written Prior Authorization:

- The beneficiary had an adverse reaction to the generic product and has documentation from the prescriber that includes one of the following:
  - The reaction was life threatening
  - Required hospitalization
  - Caused disability
  - Required intervention to prevent impairment or damage
- The beneficiary had an allergic reaction to the generic product. The prescriber must document:
  - The reaction, including dates and clinical details
  - The name of specific manufacturer of the product
  - All generic versions involved
- The beneficiary had therapeutic failure of the generic product. The prescriber must document the clinical failure due to the beneficiary's suboptimal drug plasma concentration while taking the generic drug when compared to published full pharmacokinetic profiles for the brand name drug.

## Preferred Drug List Update

Below is a list of current preferred agents. A complete list of both preferred and non-preferred agents may be found on the KHPA Web site. The Preferred Drug list may be updated at any time; please visit the KHPA Web site the most recent version.

[http://www.khpa.ks.gov/pharmacy/pharmacy\\_druglist.html](http://www.khpa.ks.gov/pharmacy/pharmacy_druglist.html)

Allergy Agents	Anti-Infectives	Central Nervous System	Injectables
<b>Non-Sedating Antihistamines</b>	<b>Anti-Herpes Virus Agents</b>	<b>Adjunct Antiepileptics</b>	<b>Erythropoiesis—Stimulating Agents</b>
Claritin® (loratadine)	Valtrex® (valacyclovir)	Keppra® (levetiracetam)	Aranesp® (darbepoetin alfa)
Claritin-D® (loratadine/pseudoephedrine)	Zovirax® (acyclovir)	Lyrica® (pregabalin)	<b>Growth Hormones</b> (Clinical PA is still required for all growth hormones)
-KBH only	-Oral Dosage Forms Only	Neurontin® (gabapentin)	Genotropin® (somatropin)
Zyrtec® (cetirizine)		Zonegran® (zonisamide)	Genotropin MiniQuick® (somatropin)
Zyrtec-D® (cetirizine/pseudoephedrine)	<b>Cardiovascular Agents</b>	<b>Non-Benzodiazepine Sedative Hypnotics</b>	Nutropin® (somatropin)
-KBH only	<b>ACE Inhibitors</b>	Lunesta® (eszopiclone)	Nutropin AQ® (somatropin)
<b>Analgesics</b>	Accupril® (quinapril)	Zolpidem (generic only)	Tev-Tropin® (somatropin)
<b>Muscle Relaxants (Skeletal)</b>	Capoten® (captopril)	<b>Non-Scheduled Novel Sleep Agents</b>	Saizen® (somatropin)
Flexeril 10mg® (cyclobenzaprine)	Lotensin® (benazepril)	Rozerem® (ramelteon)	<b>Insulin (Delivery Systems)</b>
Parafon Forte DSC® (chlorzoxazone)	Monopril® (fosinopril)	<b>Diabetic Agents</b>	All Multi-dose vials
Robaxin® (methocarbamol)	Prinivil® (lisinopril)	<b>Alphaglucohydrolase Inhibitors</b>	<b>Nasal Agents</b>
Robaxin-750® (methocarbamol)	Vasotec® (enalapril)	Glyset® (miglitol)	<b>Intranasal Corticosteroids</b>
Robaxinai® (methocarbamol/aspirin)	Zestril® (lisinopril)	<b>Biguanides</b>	Flonase® (fluticasone)
<b>Muscle Relaxants (Spasticity)</b>	<b>ACE Inhibitor/Calcium Channel Blocker Combos</b>	Glucophage® (metformin)	Nasonex® (mometasone)
Lioresal® (baclofen)	Lotrel® (benazepril/amlodipine)	Metformin Extended Release (generics only)	Rhinocort AQ® (budesonide)
Zanaflex® (tizanidine)	<b>ARBs</b>	<b>Meglitinides</b>	Veramyst® (fluticasone)
-Tablets Only	Avapro® (irbesartan)	Starlix® (nateglinide)	<b>Ophthalmic Agents</b>
<b>Non-Steroidal Anti-Inflammatory</b>	Avalide® (irbesartan/HCTZ)	<b>2<sup>nd</sup> Generation Sulfonylureas</b>	<b>Ophthalmic Prostaglandin Analogs</b>
Advil® (ibuprofen)	Cozaar® (losartan/HCTZ)	Amaryl® (glimepiride)	Travatan® (travoprost)
Aleve® (naproxen)	Diovan® (valsartan)	DiaBeta® (glyburide)	Travatan Z® (travoprost)
Anaprox® (naproxen sodium)	Diovan HCT® (valsartan/HCTZ)	Glucotrol® (glipizide)	Xalatan® (latanoprost)
Anaprox DS® (naproxen sodium)	Hyzaar® (losartan)	Glucotrol XL® (glipizide XL)	<b>Osteoporosis Agents</b>
Ansaic® (flurbiprofen)	Micardis® (telmisartan)	Glucovance® (glyburide/metformin)	<b>Bisphosphonates</b>
Arthrotec® (diclofenac/misoprostol)	Micardis HCT® (telmisartan/HCTZ)	Glynase PresTab® (glyburide micronized)	Actonel® (risedronate)
Cataflam® (diclofenac potassium)	<b>Beta-Blockers</b>	Micronase® (glyburide)	Fosamax® (alendronate)
Clinoril® (sulindac)	Betapace® (sotalol)	<b>Thiazolidinediones</b>	Fosamax Plus D® (alendronate/cholecalciferol)
Daypro® (oxaprozin)	Betapace AF® (sotalol AF)	Actos® (pioglitazone)	<b>Respiratory</b>
EC-Naprosyn® (naproxen)	Blocadren® (timolol)	ACTOplus Met® (pioglitazone/metformin)	<b>Inhaled Corticosteroids</b>
Lodine® (etodolac)	Corgard® (nadolol)	Avandamet® (rosiglitazone/metformin)	Azmacort® (triamcinolone)
Lodine XL® (etodolac)	Coreg® (carvedilol)	Avandaryl® (rosiglitazone/glimepiride)	Flovent® (fluticasone)
Meclomen® (meclofenamate)	Coreg CR® (carvedilol CR)	Avandia® (rosiglitazone)	Pulmicort Flexhaler® (budesonide)
Mobic® (meloxicam)	Inderal® (propranolol)	Duetact® (pioglitazone/glimepiride)	Pulmicort Respules® (budesonide)
Motrin® (ibuprofen)	InnoPran XL® (propranolol XL)	<b>Gastrointestinal Agents</b>	-6 & under only
Motrin IB® (ibuprofen)	Kerlone® (betaxolol)	<b>H<sub>2</sub> Antagonists</b>	QVAR® (beclomethasone)
Nalfon® (fenopropfen)	Lopressor® (metoprolol tartrate)	Axid® (nizatidine)	<b>Long Acting Inhaled Beta<sub>2</sub> Agonists</b>
Naprelan® (naproxen sodium)	Propranolol Intensol® (propranolol)	Axid AR® (nizatidine)	Foradil® (formoterol)
Naprosyn® (naproxen)	Sectral® (acebutolol)	Pepcid® (famotidine)	Serevent® (salmeterol)
Orudis® (ketoprofen)	Tenormin® (atenolol)	Zantac® (ranitidine)	<b>Short Acting Inhaled Beta<sub>2</sub> Agonists</b>
Orudis KT® (ketoprofen)	Toprol XL® (metoprolol succinate)	<b>Proton Pump Inhibitors</b>	Maxair® (pirbuterol)
Oruvail® (ketoprofen)	Visken® (pindolol)	Kapidex® (dextansoprazole)	ProAir HFA® (albuterol)
Toradol® (ketorolac)	<b>Calcium Channel Blockers (Dihydropyridines)</b>	Omeprazole OTC (omeprazole magnesium)	Proventil® (albuterol)
-limit 5 day supply	Adalat CC® (nifedipine ER)	Prevacid® (lansoprazole)	Proventil HFA® (albuterol)
Tolectin DS® (tolmetin)	Cardene® (nifedipine IR)	Prevacid OTC® (lansoprazole)	Ventolin® (albuterol)
Tolectin 600® (tolmetin)	DynaCirc® (isradipine IR)	Prilosec OTC® (omeprazole magnesium)	Ventolin HFA® (albuterol)
Voltaren® (diclofenac sodium)	DynaCirc CR® (isradipine CR)	<b>Serotonin 5HT<sub>3</sub> Antagonists</b>	<b>Urologic Agents</b>
Voltaren XR® (diclofenac sodium)	Norvasc® (amlodipine)	Zofran® (ondansetron)	<b>Anticholinergics</b>
<b>Triptans</b>	Procordia XL® (nifedipine ER)	Zofran ODT® (ondansetron)	Detrol® (tolterodine)
Amerge® (naratriptan)	Sular® (nisoldipine)	<b>Gout Agents</b>	Detrol LA® (tolterodine LA)
Frova® (frovatriptan)	<b>Calcium Channel Blockers (Non-Dihydropyridines)</b>	<b>Xanthine Oxidase Inhibitors</b>	Ditropan® (oxybutynin)
Imitrex® (sumatriptan)	Calan® (verapamil IR)	Zyloprim® (allopurinol)	Ditropan XL® (oxybutynin XL)
Maxalt® (rizatriptan)	Calan SR® (verapamil SR)		Enablex® (darifenacin)
Relpax® (eletriptan)	Cardizem® (diltiazem IR)		Toviaz® (fesoterodine)
<b>Antihyperlipidemics</b>	Covera HS® (verapamil ER)		
<b>Fibric Acid Derivatives</b>	-Brand Name Only		
Fenofibrate® (fenofibrate)	Diltia XT® (diltiazem SR)		
Lipid® (gemfibrozil)	-& AB Rated Generics		
TriCor® (fenofibrate)	Isoprin SR® (verapamil SR)		
<b>HMG-CoA Reductase Inhibitors (Statins)</b>	Tiazac® (diltiazem)		
Crestor® (rosuvastatin)	-& AB Rated Generics		
Lipitor® (atorvastatin)	Verelan® (verapamil SR)		
Zocor® (Simvastatin)			

This list was updated on 11/25/09—Please visit the KHPA Web site for the most current version.

## Understanding Bioequivalence

*Continued from Page 1.*

There are clinical anecdotes of patients who experienced clinical deterioration or toxic side effects when they were switched from a brand name drug to a generic drug. The FDA's Therapeutic Inequivalence Action Coordinating Committee (TIACC) investigates reports of generic drugs not being bioequivalent to their brand name counterparts. According to TIACC, when a generic drug has been manufactured in accordance with FDA good manufacturing practices, it is often difficult to find any scientific evidence to support this claim, even for some published cases of supposed lack of bioequivalence. However, when a report reveals problems regarding quality that are substantiated through investigation, appropriate actions are taken. These may include recommendations for product recall, withdrawal, or reclassification of its therapeutic equivalence code.

### Conclusion

Although there are anecdotal reports of adverse effects when patients switch from brand name to generic products, there is no proof that therapeutically-equivalent drugs would differ in efficacy. In the overwhelming number of cases, generic drugs are bioequivalent and clinically equivalent to the brand name product. In rare cases, adverse effects have been noted when a generic product is used in place of a brand name; an example would be an allergy to an inactive ingredient. In these cases, an authorized generic or branded generic (the actual brand name drug product relabeled and marketed under a generic name), if available, should be considered.



Health Information Designs, Inc. (HID) provides drug utilization review and pharmacy benefit management services. We specialize in helping our clients promote clinically-appropriate and cost effective prescribing, dispensing, and utilization of prescription drugs.

For 33 years, HID has worked to improve the quality and cost effectiveness of healthcare through the clinically rational use of prescription medication. Our clients include public and private healthcare plans throughout the U.S., with a combined total of over 14 million covered lives.

Health Information Designs, Inc. was founded in 1976 and is incorporated as a C Corporation in the State of Delaware. HID's initial mission was to market drug utilization review (DUR) services nationally and since its founding, has provided DUR services for clients in approximately one-half of the United States. HID is headquartered in Auburn, Alabama, with regional offices in Arkansas, Maryland, and Mississippi.

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